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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,565	10/11/2001	Catherine S. Levisage	55322 (71699)	7490

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,565	LEVISAGE ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,37-42,52 and 53* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 14-20, 37-42, 52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, 1.132 declaration, request for reconsideration and remarks, all filed 05/31/05. Claims 1-20, 37-42, 52 and 53 are pending. No claim was amended with this submission. Claims 12 and 13 are withdrawn from consideration.

Claim Rejections - 35 USC § 103

1. Claims 1-11, 14-20, 37-42, 52 and 53 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bru-Magniez et al. (US 6,211,273).

Applicants' argument is centers around the 132 declaration regarding the particle size and also that instant claim 37 is directed to a method of treating urological disease or disorder by administering intravesically a microparticle having a particle size of between about 1.0 μm and 100 μm. Applicants further state that larger particles remain in the bladder after intravesical administration without being eliminated in the urine stream and without being transported from the bladder to the other organs or tissues. Furthermore, applicants state that nanoparticles of poly(phosphoester) poly(D,L-lactide-co-ethyl phosphate) having a mean particle size of 600 nm and composed of DNA are transported to the lymph nodes shortly after intravesical administration in the bladder while microparticles having a mean particle size of about 5 mm are retained in the bladder. Applicants conclude/infer from the preceding that microparticles retained in the bladder are particularly suited to the delivery of therapeutics in the treatment or prevention of urological disorder.

2. Applicants' arguments filed 05/31/05 have been fully considered but they are not persuasive.

Regarding the particle size, Bru-Magniez discloses particle size of 100 nm (0.1μm) to 500 nm (0.5 μm) while the particle size in claim 1 is about 1.0 μm to about 100 μm. About 1.0 μm does not include 1.0 μm and 0.1 μm is less than about 1.0 μm and less than 0.5 μm is closer to 1.0 μm, the lower particle size limit of applicants' microparticle. The Experiment 4.2 of Dr. Leong's declaration uses 600 nm and while the prior art uses particle of less than 500 nm. The microparticles in Example 4.4 is directed to P(DAPG-EOP), which is not the polymer in the claims. The Examples in the declaration do not describe how much drug is released but the Examples rather discuss retention of the polymer in the bladder lumen. Although, applicants infer that microparticles retained in the bladder are suited for delivery of therapeutics, it is noted that there is no experimental correlation between retention of the polymer and how much drug is delivered or released to the lumen of the bladder. The experiment does not show drug release from particles of less than 0.5 μm and particles of about 1.0 μm. There is no study showing the correlation of retention of the polymer and drug delivery. The method is one of administration and the prior art administers.

Response to Declaration of Dr. Kam Leong

The Experiment 4.2 of Dr. Leong's declaration uses 600 nm and while the prior art uses particle of less than 500 nm. The microparticles in Example 4.4 is directed to P(DAPG-EOP), which is not the polymer in the claims. The Examples in the declaration do not describe how much drug is released but the Examples rather discuss retention of the polymer in the bladder lumen. Although, applicants infer that microparticles retained in the bladder are suited for delivery of therapeutics, it is noted that there is no experimental correlation between retention of the polymer and how much drug is delivered or released to the lumen of the bladder. The

experiment does not show drug release from particles of less than 0.5 μm and particles of about 1.0 μm. There is no study showing the correlation of retention of the polymer and drug delivery.

P(DAPG-EOP) is not one of the polymers on the examined claims and if one embodiment meets one of the repeat uints of the claim, it is also noted that that particular polymer may be at best one of the possibilities. Claim 1 does not recite double emulsion technique of preparing the composition of claim 1 and claim 4 is directed to product produced by single emulsification process; thus the Experiment 4.1 discussing double emulsion process is not commensurate with the claims. The declaration makes reference to PCT WO 99/55309 while the cited reference is US 6,211,273.. In Example 5.2 of the declaration, an 8-week old mice is used in the experiment. In all the experiments in the declaration, the retention of the polymer in the bladder are described and not the release profile of the drugs; there is also no correlation of the retention with the delivery of drug. The claims are not directed to retention of polymer in the lumen of the bladder, but rather, in instant claim 37, sustained release of drug after administration of the polymer.

No claim is allowed.

The text of the previous 35 USC 103 rejection is provided below.

Bru-Magniez discloses a nanoparticles of polymeric support material network within which therapeutic agents such as taxol and 5-fluorouracil are dispersed (abstract, column 2, lines 35-50, column 5, lines 3-35 and column 6, lines 25-36). The disclosed polymer network meets the polymer structure of the instant claims and the prior art specifically discloses methylidene malonate nanoparticles (column 2, lines 15-17 and Title). The instant method comprises

administering the polymeric composition. The prior art administers the composition orally, sublingually, subcutaneously, intramuscularly, intravenously, transdermally, locally, rectally, via the pulmonary route, or nasally; preferred forms of administration notably comprise oral forms, such as tablets, gelatin capsules, powders, granules and oral solutions or suspensions, sublingual and buccal administration forms, as well as subcutaneous, intramuscular intravenous, intranasal or intraocular and rectal administration forms (column 6, lines 43-53). It is inherent that the administered composition comprising an anticancer drug would inherently provide the desired effect. The nanoparticles of Bru-Magniez have diameter of less that 500 nm and particles having diameter of 100-500 nm are preferred (column 3, line 67 to column 4 line 1). The method of preparing the particles of Bru-Magniez involves preparing a solution of the polymer in a water miscible organic solvent, adding with stirring, the organic phase to an aqueous polymerization medium at a pH between 4.5 and 10, homogenizing the mixture, evaporating the organic solvent in vacuo to recover/collect the nanoparticles (column 4, lines 5-13). In another embodiment, the polymer precipitates in the polymerization medium, the polymer is recovered by filtration and the suspension or filtrate of the nanoparticles is "conditioned and lyophilized" (column 4, lines 14-36). It is noted that the process of recovering precipitates by filtration routinely involves wash cycle(s).

Bru-Magniez discloses the composition and method for preparing the composition. The difference between the prior art and the instant claims is the size of the particles. The prior art discloses particle diameter of less than 500 nm, which is 0.5 μm. The amended claim now has a lower limit of 1.0 μm and applicants' specification and the remarks provide no demonstration that a microparticle having a mean particle diameter of about 1.0 μm provides unusual results. A

mean particle diameter of about 1.50μm is not critical over a mean particle diameter of less than 0.5 μm in the absence of a showing of criticality. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the nanoparticle of Bru-Magniez. One having ordinary skill in the art would have been motivated to prepare nanoparticles of methylidene malonate having a diameter of less than 500 nm or 100-500 nm with the expectation that the medicament dispersed within the polymer is delivered to a subject.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BF

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